

THE STUDY OF MINOR PHENOTYPIC ABNORMALITIES IN CORNELIA DE LANGE SYNDROME

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Abstract

The purpose of my study is to identify minor phenotypic abnormalities, such as those of hair and to establish a specific association between these abnormalities and certain genetic syndromes. Two groups of children were studied, out of which a group of children diagnosed with Cornelia de Lange syndrome, who were registered with the Department of Medical Genetics in Oradea. Also, a control sample was made up of children hospitalized in the Clinic of Pediatrics from Oradea, namely non-serious cases, hospitalized for transient intercurrent pathology. The incidence of hair phenotypic anomalies has significantly increased in patients with genetic diseases, as compared with the general population, the results were consistent with some data in the specialty literature. Associations of multiple phenotypic abnormalities were found. The study of clinical dysmorphology with detailed description of phenotypic abnormalities, including those considered minor, such as those of hair, proved essential in deciphering the many genetic syndromes. Many genetic disorders are associated with air anomalies, that is why its investigation is considered a diagnostic tool very simple, handy and especially useful in pediatrics, genetics and dermatology.

INTRODUCTION

Hair phenotypic anomalies represent minor abnormalities whose presence or absence serves as an indicator of events during embryological development. Although from a medical point of view many anomalies do not have a significant impact, taken together these minor anomalies represent evidence of a development dynamics with negative impact on morphogenesis. The association of multiple minor anomalies increases the risk of major malformations. (Margaret Adam, et. al., 2003)

Disorders affecting hair density, meaning hair loss or excessive growth on the face or body, and also its quality affects not only the looks of a person, most of the times they have an emotional impact particularly with impaired quality of life, social isolation, low self-esteem and sometimes even mental disorders.

Although many times life span in the case of these abnormalities is not affected, the major impact is felt on the patient's personal and social life.

Cornelia de Lange syndrome (Brachmann-de Lange syndrome) is a complex developmental disorder that consists of characteristic facial features, limb abnormalities, hypertrichosis, gastroesophageal dysfunction,

hearing loss, eye diseases, neurological disorders and growth. (LM Malik et. al., 2011, Uzun H. et. al.2008). More than 99% of cases are sporadic, rarely it is transmitted autosomal dominant. The cause is a heterozygous mutation at the level of NIPBL gene on chromosome 5p13. (Rohatgi Sarika. et. al. 2010, Liu J et. al. 2010 Musio, A et. al.2006). Both sexes are equally affected. Diagnosis is determined at birth based on clinical examination, in which hairiness appearance is suggestive: generalized hypertrichosis, especially on the back, shoulders, extremities, long eyelashes, thick, long, thick, well-defined, thick, joined in the midline eyebrows (Synophrys), front and rear low insertion of hair. (Die-Smulders C et. al. 1992 Luzzana S et. al. 1993, Bay, C.et. al. 1993, Berney, T. P et. al. 1999).

The aim of my study is to analyze the phenotypic abnormalities of hair associated with Cornelia de Lange syndrome pursuing the type of anomalies, the frequency with which they occur and to compare these data with the results obtained from the study of the control group and those described in the literature.

MATERIAL AND METHOD

To study the hair phenotypic features in the case of children with genetic pathology we conducted a retrospective study on a group of 14 children who were registered with the Department of Medical Genetics in Oradea.

Patients were included in the study based on the following criteria:

1. patients diagnosed with Cornelia de Lange syndrome
2. patients who were registered with the Department of Medical Genetics in Oradea
3. patients with complete and accessible medical documentation required, as well as related photo documentation

The exclusion criteria have included cases for which we did not possess the complete medical documentation.

Based on these criteria we included in the study group a total number of 14 children with genetic disorders mentioned, five boys and nine girls. (Figure 1)

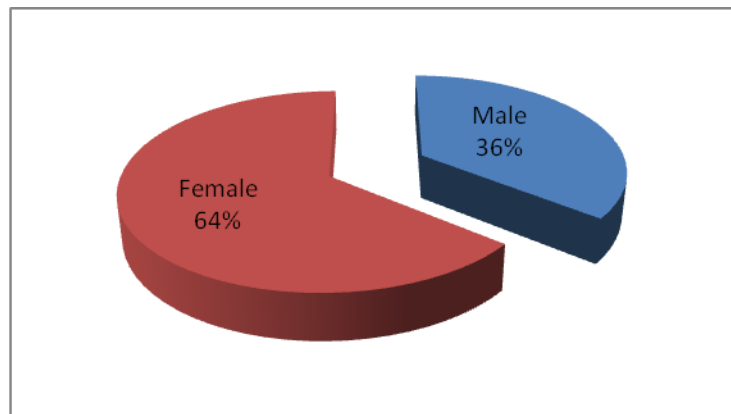


Fig. 1. Representation of the study group in percentages

The age of patients included in the study ranged between 0 and 34, inclusive, as follows: 1 – 3 years: 2 cases, 7 – 10 years: 4 cases, 11 – 14 years: 3 cases, 15 – 18 years: 1 case, more than 18 years: 4 cases. (Figure 2)

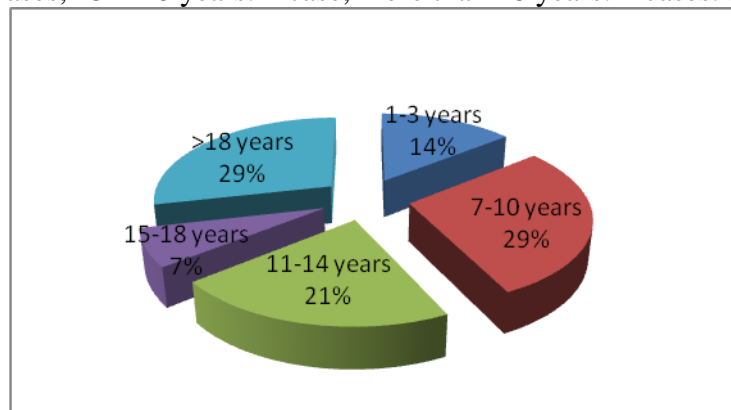


Fig. 2. Distribution of patients according to age

A total number of 4 patients were coming from urban areas and 10 from rural areas.

The control group constituted for the comparative analysis of the cases consisted of 14 subjects comparable with regard to age, sex, area of origin as patients with genetic pathology included in the study group. The subjects of control group were recruited randomly between patients from the Pediatrics Clinic Oradea, namely non-serious cases, hospitalized for transient intercurrent pathology.

The classification of traced phenotypic abnormalities was done according to the international classification published in London Dysmorphology Data Base, in which they are classified into anatomical

variants, minor phenotypic abnormalities and proper malformations. (Winter RM, Baraitser M., 2001)

RESULTS AND DISCUSSIONS

Within the study group, the phenotypic abnormalities present were represented by quantitative and insertion of hair anomalies, namely: hypertrichosis, predominantly in the back and limbs (in 14/14 patients), low insertion of hair at the level of forehead and neck in 10/14 patients, long eyelashes in 13/14 patients, Synophrys for 11/14 patients, thick eyebrows, thick in 10/14 patients. (Table 1)

Table 1

Presentation of hair phenotypic abnormalities in the case of the study group

	Hypertrichosis	Low insertion of hair	Long eyelashes	Synophrys	Thick eyebrows
Study group (14 patients)	14 / 14	10 / 14	13 / 14	11 / 14	10 / 14

In the case of the control group there were no abnormalities of the kind included in this study. (Table 2)

Table 2

Presentation of results obtained in the case of the study group compared to the control group and speciality literature

	Hypertrichosis	Low insertion of hair	Long eyelashes	Synophrys	Thick eyebrows
Study group	100 %	71 %	92 %	78 %	71 %
Control group	-	-	-	-	-
Specialty literature	100 %	72 %	99 %	98 %	frequent

Hair phenotypic abnormalities occur with increased frequency in Cornelia de Lange syndrome. (Jones KL, 2006, Hei MY et. al.2012, Ireland, M et. al. 1993, J E Allanson et. al. 1997). The increased incidence of this type of anomalies is proven through clinical studies published in the literature. (McArthur, R. G et. al. 1967, Hawley, P. P. Et. al. 1985, Caksen, H et. al. 2001, Filippi, G. 1989, Greenberg, F et. al. 1989)

In the control group there were no abnormalities of the kind studied.

Among the anomalies studied, quantitative abnormalities showed a higher frequency compared to the insertion of hair anomalies.

All patients in the study group had multiple hair phenotypic abnormalities, none of the anomalies mentioned were not present in isolation.

It was noted a higher frequency of phenotypic abnormalities in males versus female.

CONCLUSIONS

The studied phenotypic abnormalities are present only in the study group. In the case of the studied syndrome they are common, their incidence exceeding 71%.

The study of clinical dysmorphology with a detailed description of phenotypic abnormalities, including those of hair, proved essential in deciphering the many genetic syndromes.

Many genetic disorders are associated with abnormalities of hair, that is why its investigation is considered a simple and handy diagnostic tool, especially useful especially in pediatrics, genetics and dermatology.

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